

# Exhibit 6

# Transvaginal mesh repair of anterior or posterior vaginal wall prolapse

Interventional procedures guidance

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[nice.org.uk/guidance/ipg599](https://nice.org.uk/guidance/ipg599)

## Your responsibility

This guidance represents the view of NICE, arrived at after careful consideration of the evidence available. When exercising their judgement, healthcare professionals are expected to take this guidance fully into account. However, the guidance does not override the individual responsibility of healthcare professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and/or guardian or carer.

Commissioners and/or providers have a responsibility to implement the guidance, in their local context, in light of their duties to have due regard to the need to eliminate unlawful discrimination, advance equality of opportunity, and foster good relations. Nothing in this guidance should be interpreted in a way that would be inconsistent with compliance with those duties.

Commissioners and providers have a responsibility to promote an environmentally sustainable health and care system and should assess and reduce the environmental impact of implementing NICE recommendations wherever possible.

This guidance replaces IPG267.

## 1 Recommendations

- 1.1 Current evidence on the safety of transvaginal mesh repair of anterior or posterior vaginal wall prolapse shows there are serious but well-recognised safety concerns. Evidence of long-term efficacy is inadequate in quality and quantity. Therefore, this procedure should only be used in the context of research.
- 1.2 All adverse events involving the medical devices (including the mesh) used in this procedure should be reported to the [Medicines and Healthcare products Regulatory Agency](#).
- 1.3 Further research should include details of patient selection, long-term outcomes including complications, type of mesh used and method of fixation, and quality of life.

## 2 Indications and current treatments

- 2.1 Vaginal wall prolapse is a protrusion of 1 or more pelvic organs (such as the bladder or the rectum) through the vaginal fascia. The vaginal wall then moves from its normal position (prolapses), into or outside the vagina. Vaginal wall prolapse can affect a woman's quality of life because of its local physical effects (pressure, bulging, heaviness or discomfort). It can also affect urinary, bowel or sexual function. There are different types of vaginal wall prolapse depending on the organs and sites involved. These include anterior vaginal wall prolapse (including prolapse of the urethra [urethrocele] or bladder [cystocele]) and posterior vaginal wall prolapse (including prolapse of the rectum [rectocele] or small bowel [enterocele]). A woman can present with prolapse of 1 or both of these sites.
- 2.2 Current treatment options for vaginal wall prolapse include pelvic floor muscle training, use of mechanical devices (ring or shelf pessaries) and surgery, including anterior or posterior colporrhaphy and site-specific defect repair such as paravaginal repair.
- 2.3 The aims of using mesh to repair vaginal wall prolapse are to add extra support and to reduce the risk of recurrence, particularly for women with recurrent

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prolapse or with congenital connective tissue disorders (such as Ehlers–Danlos syndrome or Marfan's syndrome).

### 3 The procedure

- 3.1 Transvaginal mesh repair of anterior or posterior vaginal wall prolapse involves removing some of the stretched tissue if needed, and tightening the underlying tissue (colporrhaphy). Mesh is used to support the repair.
- 3.2 The procedure is usually done with the patient under general anaesthesia. Anterior colporrhaphy involves dissection of the vaginal mucosa through a midline incision in the anterior vaginal wall to expose the bladder and pubocervical fascia. The fascia is then plicated (folded), some excess tissue may be removed and the incision is closed. Posterior colporrhaphy involves a vaginal incision and plication of the levator ani. Other site-specific procedures, such as paravaginal repair, may also be done using methods similar to colporrhaphy.
- 3.3 The technique for inserting mesh varies. Mesh is usually placed using an open technique, although trocar introducers can also be used without direct visualisation. The mesh is usually positioned and sutured over the fascial defect as an 'inlay'.

### 4 Efficacy

This section describes efficacy outcomes from the published literature that the committee considered as part of the evidence about this procedure. For more detailed information on the evidence, see the [interventional procedure overview](#).

- 4.1 In a randomised controlled trial (RCT) of 865 women with anterior or posterior vaginal wall prolapse treated by synthetic mesh augmented repair or standard repair alone, there were no statistically significant differences in prolapse symptom scores (5.3 versus 4.9 respectively,  $p=0.37$ ). There were also no statistically significant differences in symptomatic prolapse (85% [291/341] compared with 82% [283/347] respectively,  $p=0.30$ ) or the proportion of women reporting 'something coming down' (34% [116/342] compared with 31% [106/347] respectively,  $p=0.59$ ) at 2-year follow-up. The quality-of-life scores were also similar. In an RCT of 735 women with anterior or posterior vaginal wall prolapse treated by biological graft augmented repair or standard

repair alone, there were no statistically significant differences in prolapse symptom scores (5.5 compared with 4.9 respectively,  $p=0.43$ ) or symptomatic prolapse (82% [245/299] compared with 81% [242/298] respectively,  $p=0.85$ ). The proportion of women reporting 'something coming down' was statistically significantly higher in the graft augmented repair group (40% [120/299] compared with 31% [91/298] in the standard repair alone group,  $p=0.04$ ) at 2-year follow-up. The quality-of-life scores were similar between the 2 groups.

- 4.2 In a systematic review of 4,023 patients, there was a statistically significantly lower risk of awareness of prolapse in women treated by transvaginal permanent mesh repair compared with native tissue repair (relative risk [RR] 0.66, 95% confidence interval [CI] 0.54 to 0.81;  $n=1,614$ , 12 RCTs) at 1- to 3-year follow-up.
- 4.3 In the RCT of 865 women with anterior or posterior vaginal wall prolapse treated by synthetic mesh augmented repair or standard repair alone, there were no statistically significant differences in the proportions of women with an overall Pelvic Organ Prolapse Quantification (POP-Q) score of 2b, 3 or 4 (16% [54/336] compared with 14% [47/338] respectively,  $p=0.52$ ) at 1-year follow-up. In the RCT of 735 women with anterior or posterior vaginal wall prolapse treated by biological graft augmented repair or standard repair alone, the proportions of women with an overall POP-Q score of 2b, 3 or 4 were 18% (54/298) and 16% (47/303) respectively at 1-year follow-up ( $p=0.47$ ). In the systematic review of 4,023 patients, women who had a transvaginal mesh repair were less likely to have a stage 2 or worse anterior compartment prolapse on examination than those having a native tissue repair (RR 0.45, 95% CI 0.36 to 0.55, 13 RCTs,  $n=1,406$ ,  $I^2=35\%$ ) at 1- to 3-year follow-up. The risk of recurrent prolapse was lower in the transvaginal permanent mesh group than in the native tissue repair group (RR 0.40, 95% CI 0.30 to 0.53, 21 studies,  $n=2,494$ ,  $I^2=73\%$ ).
- 4.4 In the systematic review of 4,023 patients, those who had a transvaginal mesh repair were less likely to have repeat surgery for prolapse (RR 0.53, 95% CI 0.31 to 0.88, 12 RCTs,  $n=1,675$ ) at 1- to 3-year follow-up than those who had native tissue repair. In a population-based cohort study of 27,809 patients who had mesh or native tissue repair, surgery for recurrent prolapse was reported in similar proportions of patients: 5% of patients in both groups at 1-year follow-up, and 10% (95% CI 9 to 12%) in the mesh group at 5-year follow-up compared with 9% (95% CI 9 to 10%) in the native tissue group. In the RCT of

865 patients who had synthetic mesh or standard repair, further prolapse surgery was needed in a similar proportion of patients (4% [15/343] compared with 5% [16/348] respectively) at 2-year follow-up. In the RCT of 735 patients who had biological graft or standard repair, further prolapse surgery was needed in 5% of patients in both groups (15/300 and 15/299) at 2-year follow-up.

- 4.5 The specialist advisers listed anatomical success, restoration of bladder, bowel and sexual function, and long-term success as the key efficacy outcomes.
- 4.6 Sixteen commentaries from patients who had experience of this procedure were received, which were discussed by the committee.

## 5 Safety

This section describes safety outcomes from the published literature that the committee considered as part of the evidence about this procedure. For more detailed information on the evidence, see the [interventional procedure overview](#).

- 5.1 Immediate postoperative complications were reported in 4% (20/278) of patients who had anterior prolapse repair with mesh and 4% (343/7643) of patients who had repair without mesh in a cohort study of 18,986 patients. Late postoperative complications were more common in patients who had a mesh repair compared with those who had a non-mesh repair (adjusted incidence rate ratio 3.15, 95% confidence interval [CI] 2.46 to 4.04) in the same study.
- 5.2 Mesh complications were reported in 12% (51/434) of patients who had a synthetic mesh repair at 2-year follow-up in a randomised controlled trial (RCT) of 865 patients. Surgical removal of the mesh was needed in 9% (37/434) of patients in the same study. Mesh complications were reported in less than 1% (2/368) of patients who had a biological graft repair and less than 1% (2/367) of patients who had a standard repair in an RCT of 735 patients. Surgical removal was needed in 3 of the 4 patients. Surgery for mesh complications was reported in 6% of patients who had a mesh repair in a cohort study of 27,809 patients.
- 5.3 Mesh exposure was reported in 12% (134/2,097) of patients who had a transvaginal permanent mesh repair in a systematic review of 4,023 patients at 1- to 3-year review. Surgery for mesh exposure was reported in 8% (100/1,227)

of patients in the same review. The overall rate of graft erosion (by meta-analysis of 110 studies) was 10% (95% CI 10 to 11%) of procedures in a systematic review of 126 studies. Mesh erosion was reported in 5% (32/677) of patients and vesicovaginal fistula with mesh extrusion was reported in less than 1% of patients (2/677) in a case series of 677 patients.

- 5.4 Serious adverse effects of any kind (excluding mesh complications) were reported in 8% (34/435) of patients who had a synthetic mesh repair and 7% (31/430) of patients who had a standard repair ( $p=0.73$ ) at 1-year follow-up in the RCT of 865 patients. Serious adverse effects of any kind (excluding mesh complications) were reported in 10% (36/368) of patients who had a biological graft repair and 6% (23/367) of patients who had a standard repair ( $p=0.08$ ) at 1-year follow-up in the RCT of 735 patients.
- 5.5 Bladder injury was more common in women who had a transvaginal permanent mesh repair than those who had a native tissue repair (relative risk [RR] 3.92, 95% CI 1.62 to 9.50, 11 RCTs,  $n=1,514$ ,  $I^2=0\%$ , moderate-quality evidence) in the systematic review of 4,023 patients. Bowel injury was reported in 1 study in the same systematic review, and there was no evidence of a difference between the 2 groups (RR 3.26, 95% CI 0.13 to 78.81,  $n=169$ ). Bladder injury and rectal damage were reported in 2% (11/677) and 1% (5/677) of patients respectively in a case series of 677 patients. In 2 patients, urinary tract injury was not recognised at the time of surgery and led to stone formation. One patient needed a laparotomy and removal of the mesh with resection of the bladder wall. Ureteric trauma was reported in 1 patient in the same study; this was treated by ureteroneocystotomy.
- 5.6 Bleeding more than 500 ml was reported in 2% (15/677) of patients in the case series of 677 patients. Vaginal or pelvic haematoma was reported in 6% (37/677) of patients in a case series of 677 patients. In 10 patients, major vaginal haematomas led to urinary retention or transformed into an abscess. Several of them needed to be drained transcutaneously. Perineal haematoma was reported in 3% (17/677) of patients in the same study.
- 5.7 Pelvic abscess was reported in 1% (4/677) of patients in the case series of 677 patients. One patient, with a history of intrauterine device inserted 30 years ago, had necrotising fasciitis. The patient developed signs of systemic

toxicity 6 days after the prolapse repair. She was treated by fasciotomy and debridement but died after 18 days.

- 5.8 De novo stress urinary incontinence was more common in patients who had a transvaginal permanent mesh repair than in those who had a native tissue repair (RR 1.39, 95% CI 1.06 to 1.82, 12 RCTs, n=1,512,  $I^2=0\%$ , low-quality evidence) in the systematic review of 4,023 patients. Incontinence surgery admissions were more common after anterior repair with mesh than after anterior repair without mesh (adjusted incidence rate ratio 3.20, 95% CI 2.06 to 4.96) in a cohort study of 18,986 patients.
- 5.9 Urinary retention within 90 days was more common in patients who had a mesh repair than in those who had a repair without mesh (8% compared with 6%, risk ratio 1.33, 95% CI 1.18 to 1.51) in a cohort study of 27,991 patients.
- 5.10 The overall rate of dyspareunia (by meta-analysis of 70 studies) was 9% (95% CI 8 to 10%) of procedures in the systematic review of 126 studies. Pain and dyspareunia was reported in 2% (16/677) of patients in the case series of 677 patients.
- 5.11 As well as safety outcomes reported in the literature, specialist advisers are asked about anecdotal adverse events (events which they have heard about) and about theoretical adverse events (events which they think might possibly occur, even if they have never done so). For this procedure, specialist advisers did not describe any additional anecdotal or theoretical adverse events.
- 5.12 Sixteen commentaries from patients who had experience of this procedure were received, which were discussed by the committee.

## 6 Committee comments

- 6.1 There are many different types of mesh in use, which have variable physical properties. New materials, including newer lightweight mesh, have been developed.
- 6.2 The surgical technique and method of fixation are important.



- 6.3 The mesh implant is intended to be permanent. If removal of mesh is needed, it can be technically difficult.
- 6.4 Randomised controlled trial data showed no added benefit of using mesh compared with native tissue repair.
- 6.5 The committee noted from consultation comments that when complications occur, these can be serious and have life-changing consequences.
- 6.6 Most commentaries received from patients reported satisfaction with the procedure and that it had worked and improved their quality of life.
- 6.7 A NICE guideline on [managing urinary incontinence and pelvic organ prolapse in women](#) is in development and is due to publish in 2019.

## 7 Further information

- 7.1 For related NICE guidance, see the [NICE website](#).

### *Information for patients*

NICE has produced information on this procedure for patients and carers ([information for the public](#)). It explains the nature of the procedure and the guidance issued by NICE, and has been written with patient consent in mind.

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### *Endorsing organisation*

This guidance has been endorsed by [Healthcare Improvement Scotland](#).

## Accreditation

